

## **REMARKS**

### **1. Claims**

Claims 67-69, 73-85, 87, 90-110, 112 and 113 are pending in this application, with claim 67 being independent.

Claims 90, 94, 95, 99-104 and 106-110 have been amended herein to more particularly point out the claimed subject matter and to delete extraneous language.

The present amendments are supported by the original disclosure and no new matter has been added. The above amendments should not be construed as constituting any admission with respect to the patentability of the previously claimed subject matter, and Applicants reserve the right to pursue any canceled subject matter in one or more continuing patent applications.

### **2. The Rejection of Claims 67-69, 73-85, 90-110, 112 and 113 under 35 USC § 103(a) is Traversed**

In the Office Action of June 20, 2006, Examiner maintains the rejection of then-pending claims 67-69, 73-85, 87, 90-110, 112 and 113 as allegedly being unpatentable over Rubin *et al.* (U.S. Pat. No. 5,925,334) in view of Schmitt *et al.* (U.S. Pat No. 4,950,477) and Saunders Manual of Medical Practice under 35 USC§ 103(a). Applicants respectfully traverse this rejection.

Examiner alleges that Rubin *et al.* teach a surfactant such as DPPC and ExoSurf<sup>®</sup> mixed with an aerosolizing agent to promote mucus clearance and that the use of such surfactants lowers the surface tension to enhance distribution and spreading of other medications such as, for example, a surfactant and an antibiotic or a surfactant and an inhaled anti-inflammatory agent for the treatment for conditions *inter alia* such as sinusitis. In addition, the Examiner alleges that Rubin *et al.* teach methods of administration of the surfactant composition via a metered dose inhaler, dry powder inhalation, jet nebulization and ultrasonic nebulization.

Contrary to the Examiner's interpretation of the disclosure of Rubin *et al.*, Applicants assert that a close analysis of the reference provides that it specifically states "...the use of surfactant to enhance the distribution of inhaled anti-inflammatory agents and bronchodilators **to the lower respiratory tract** of patients with asthma or other conditions characterized by reversible airflow obstruction due to conditions of the upper respiratory tract such as, but not limited to . . . , sinusitis" (col. 10). (Emphasis Added). Thus, in contrast to the Examiner's position, and as the Applicants

have previously asserted, Rubin *et al.* stands solely for the proposition that surfactants can lower the surface tension to enhance distribution and spreading of other medications ***to the lower respiratory tract*** and is completely void of any teaching of the use of surfactants to obtain specific surface tensions which provides for deposition, penetration, or retention of composition ***in the nasal sinuses***, as required by the presently pending claims. Moreover, Rubin *et al.* fails to teach the particle size, the osmolality, pH, or the NaCl equivalency elements required by the presently pending claims.

Examiner further alleges that the claim amendment to specify the surface tension of the composition as about 10 to 70 dynes/cm is the “mere recitation of a newly-discovered function or property, inherently possessed by things in the prior art.” Contrary to the Examiner’s allegation, Applicants assert that the cited art, individually or in combination, is completely void of the teaching of the use of surfactants to obtain specific surface tensions which provides for deposition, penetration, or retention of composition ***in the nasal sinuses***.

**(i) Examiner’s allegation of a motivation to have combined the teachings of Rubin et al. with those of Schmitt et al. and Saunders Manual to arrive at the presently claimed invention.**

On page 3 of the Office Action dated June 20, 2006, Examiner states that in holding an invention obvious in view of the combination of references, there must be some suggestion, motivation, or teaching in the prior art that would have led a person of ordinary skill in the art to select the references and combine them in the way that would produce the claimed invention. Examiner further alleges that “[H]ere, filtered through the knowledge of one skilled in the art, Rubin *et al.* disclosed that clearance of mucus in the respiratory tract can be achieved through inhalation of a surfactant combined with an aerosolizing agent and use of the surfactant lowers surface tension to surface tension to enhance distribution and spreading of other medications ***to the lower respiratory tract*** such as, for example, a surfactant and an antibiotic or a surfactant and an inhaled anti-inflammatory agent for the treatment for conditions *inter alia* such as sinusitis (Emphasis Added). Schmitt et al. teach that particle size is important because particles smaller than 0.5  $\mu\text{m}$  are exhaled and thus not retained ***in the lungs*** while particles greater than 8.0  $\mu\text{m}$  such as those produced in an atomizer ***do not reach the periphery of the lungs*** and are therefore not effective in preventing or treating infection (Emphasis Added). Saunders Manual is cited to teach the state of the art regarding the treatment of sinusitis.

**(ii) There Would Have Been No Motivation to Have Combined the Teachings of Rubin et al. With Those of Schmitt et al. and Saunders Manual to Arrive at the Presently Claimed Methods**

Contrary to the allegations of the Examiner, Applicants assert that Rubin *et al.* and Schmitt *et al.* focus on the treatment of lung conditions, such as chronic lung diseases and pulmonary infections, by solely by enhancing the penetration of an active agent into both *the lower respiratory tract* and *peripheral areas of the lung*, either by lowering the surface tension of the formulation by the addition of a surfactant or by the use of a narrow particle size range, respectively. Neither reference, singly or in combination, teaches or suggests methods for delivery of agents to *the nasal sinuses* for the treatment of chronic sinusitis. Moreover, neither reference, singly or in combination, teaches or suggests methods for the use an aqueous composition comprising betamethasone and a surfactant, wherein the composition has a surface tension of between about 10 to about 70 dynes/cm, *wherein the surface tension is effective for deposition, penetration or retention of the composition in the nasal sinuses*, whereby the aerosolized pharmaceutical composition is effective for treatment of chronic sinusitis

Thus, Applicants assert that there is no motivation or suggestion in any of the cited references to have combined the teachings of Rubin *et al.* and Schmitt *et al.* with those of the Saunders Manual to arrive at the instantly claimed methods since Rubin *et al.* and Schmitt *et al.* are concerned with solely with *enhancing deep lung penetration of an active ingredient* for the treatment of chronic lung diseases and pulmonary infections and the Saunders Manual is directed to the treatment of acute sinusitis. For at least these reasons, the Examiner has failed to meet the burden of establishing “some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings” that would produce the claimed invention. *See In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998).

Thus, the Examiner’s rejection is respectfully traversed because the Examiner has not met the burden of establishing some suggestion or motivation to combine the cited references, and even if the motivation to combine the cited references was established, which it is not, the references relied upon by the Examiner, either alone or in combination, fail to teach or suggest every element of the

Applicants' presently claimed method. Accordingly, the rejection of claims 67-69, 73-85, 87, 90-110, 112 and 11367, under 35 U.S.C. § 103(a) is improper and should be reversed.

**3. The Rejection of Claims 90, 94-97, 103, 104, 106, 108, and 109 under 35 USC § 112, First Paragraph is Obviated or Traversed**

In the Office Action of June 20, 2006, Examiner rejected claims 90, 94-97, 103, 104, 106, 108 and 109 under 35 USC § 112, first paragraph, as allegedly failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this rejection.

Examiner alleges that the recited element of 30–40 dynes/cm found in claim 90 is not found in the instant specification. Applicants assert that the Examiner has mistakenly recited 30–40 dynes/cm and intended to recite 30–50 dynes/cm. While Applicants respectfully disagree with the Examiner's position, claim 90 has been amended to recite 30–about 40 dynes/cm in the interests of gaining allowance of the claims at issue. Support for this amendment is found in the originally filed specification at page 20. Therefore, Examiner's rejection of claim 90 under 35 USC § 112, first paragraph, as allegedly failing to comply with the written description requirement is now moot.

Examiner also alleges that the recited elements of “about 400 mOsm/kg to about 700 mOsm/kg” in previously presented claim 94 and “about 500 mOsm/kg to about 600 mOsm/kg” in previously presented claim 95 are not found in the instant specification. While Applicants respectfully disagree with the Examiner's position, claim 94 has been amended to recite “about 300 mOsm/kg to about 700 mOsm/kg” and claim 95 has been amended to recite “about 400 mOsm/kg to about 550 mOsm/kg” in the interests of gaining allowance of the claims at issue. Support for these amendments is found in the originally filed specification at page 20. Therefore, Examiner's rejection of claims 94 and 95 under 35 USC § 112, first paragraph, as allegedly failing to comply with the written description requirement is now moot.

On page 6 of the Office Action dated June 20, 2006, Examiner alleges that the recited elements of a surfactant having a “hydrophile-lipophile-balance (HLB) of between about 1.8 to about 8.6” in previously presented claim 96 and “about hydrophile-lipophile-balance (HLB) of

between about 9.6 to about 16.7” in previously presented claim 97 are not supported by a description within the specification of how to make the claimed invention and therefore does not enable any person skilled in the art to make and use the claimed invention. Applicants respectfully traverse this rejection.

As the Examiner correctly notes, support for claims 96 and 97 can be found on page 24 of the specification. More specifically, on pages 23 and 24, the specification provides that exemplary surfactants include PEG 400, sodium lauryl sulfate, spans (20-40-60, etc.), tweens (polysorbates, 20-40-60, etc.), tyloxapol, propylene glycol, and benzalkonium chloride. The specification further discloses that spans have an HLB value that ranges from 1.8 to 8.6 and that tweens have an HLB value that ranges from 9.6 to 16.7. Thus, contrary to the Examiner’s position, the specification provides clear guidance on how to make and use the inventions of claims 96 or 97, i.e., by the selection of a span (HLB value that ranges from 1.8 to 8.6) or a tween (HLB value that ranges from 9.6 to 16.7) for use as a surfactant in the presently claimed invention. Moreover, a person of skill in the art, upon receiving the specific ranges of HLB values appropriate for use in the present invention, would clearly be able to determine appropriate surfactant without undue experimentation, thereby satisfying the enablement requirement under 35 USC §112, first paragraph. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313 (Fed. Cir. 2003). Accordingly, the rejection of claims 96 and 97 35 USC § 112, first paragraph is improper and should be reversed.

On pages 6 and 7 of the Office Action dated June 20, 2006, Examiner alleges that the recited elements of “about 1.1% NaCl to about 1.8 % NaCl” in previously presented claim 103 and “about 1.3% NaCl to about 1.7% NaCl” in previously presented claim 104 are not found in the instant specification. While Applicants respectfully disagree with the Examiner’s position, claim 103 has been amended to recite “about 0.45% NaCl to about 1.8% NaCl” and claim 104 has been amended to recite “about 0.9% NaCl to about 1.7% NaCl” in the interests of gaining allowance of the claims at issue. Support for these amendments is found in the originally filed specification at page 21. Therefore, Examiner’s rejection of claims 103 and 104 under 35 USC § 112, first paragraph, as allegedly failing to comply with the written description requirement is now moot.

On page 7 of the Office Action dated June 20, 2006, Examiner alleges that the recited particle size ranges of “about 3.0 to about 3.5  $\mu\text{m}$ ” in previously presented claim 106, “about 0.5 to about 5.0  $\mu\text{m}$ ” in previously presented claim 108, and “about 2.0  $\mu\text{m}$  to about 3.5  $\mu\text{m}$ ” in previously

presented claim 109 are not found in the instant specification. While Applicants respectfully disagree with the Examiner's position, claim 106 has been amended to recite "about 0.5 to about 10  $\mu\text{m}$ ". Claim 108 has been amended to recite "about 1.0 to about 5.0  $\mu\text{m}$ " and claim 109 has been amended to recite "about 2.0 to about 4.0  $\mu\text{m}$ " in the interests of gaining allowance of the claims at issue. Support for these amendments is found in the originally filed specification at page 19. Therefore, Examiner's rejection of claims 106, 108 and 109 under 35 USC § 112, first paragraph, as allegedly failing to comply with the written description requirement is now moot.

#### **4. The Rejection of Claims 99-102 and 106-110 under 35 USC § 112, Second Paragraph is Obviated**

In the Office Action of June 20, 2006, Examiner rejected claims 99-102 and 106-110 under 35 USC § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regards as the invention.

Examiner alleges that claims 99-102 and 106-110 are incomplete for omitting essential elements, such omission amounting to a gap between elements. More specifically, the Examiner alleges that the omitted element in claims 99-102 and 106-110 is the term mass median aerodynamic diameter (MMAD). While Applicants respectfully disagree with the Examiner's position, in an effort to gain allowance of the claims at issue, Applicants have amended the claims 99-102 and 106-110 to recite the term mass median aerodynamic diameter (MMAD) as suggested by the Examiner. Therefore, Examiner's rejection of claims 99-102 and 106-110 under 35 USC § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regards as the invention is now moot.

**CONCLUSION**

In view of the above amendments and remarks, reconsideration and allowance of the application are respectfully requested. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (858) 350-2307.

The Commissioner is authorized to charge any additional fees that may be required, including petition fees and extension of time fees, or credit any overpayment to Deposit Account No. 23-2415 (Attorney Docket No.: 28450-703.201).

Respectfully submitted,

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